

Applicants: Arlindo L. Castelhano, et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 2

**Amendments to the Claims**

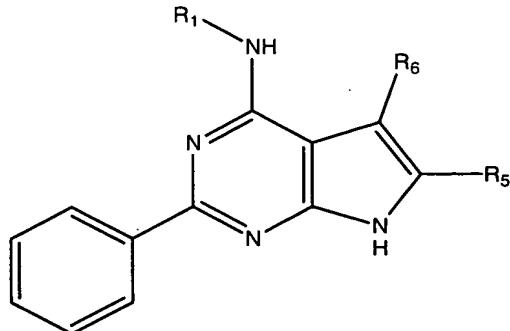
Please cancel claims 126 and 127 without disclaimer or prejudice to applicant's right to pursue the subject matter of these claims in this or a related application.

Please amend claims 76, 123, 124 and 133 under the provisions of 37 C.F.R. §1.121, as set forth in the Federal Register on June 30, 2003 as follows:

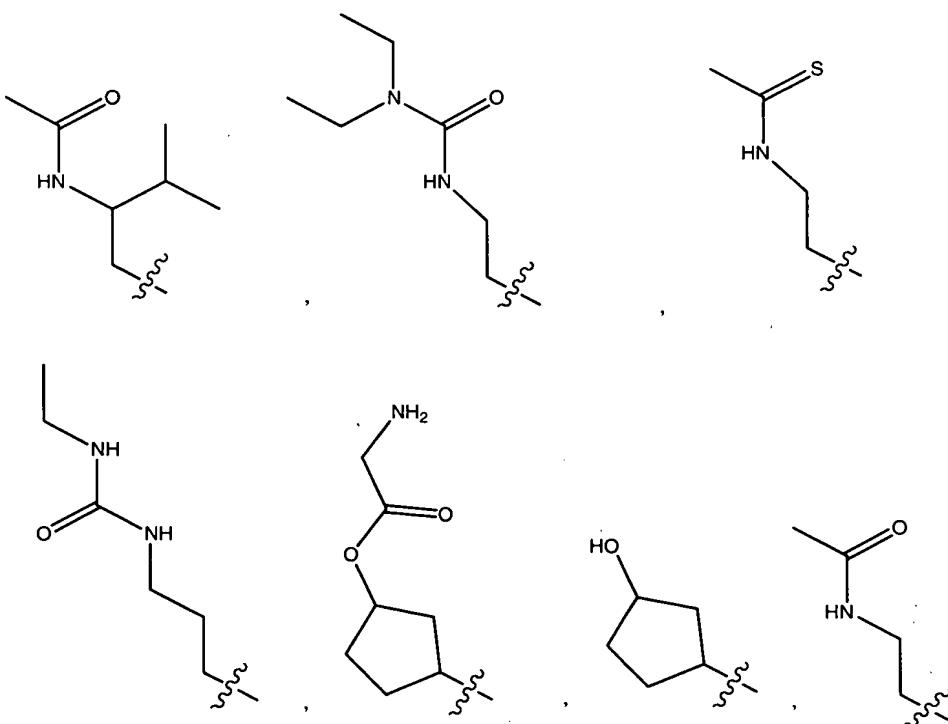
Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 3

Claims 1-75. (Canceled)

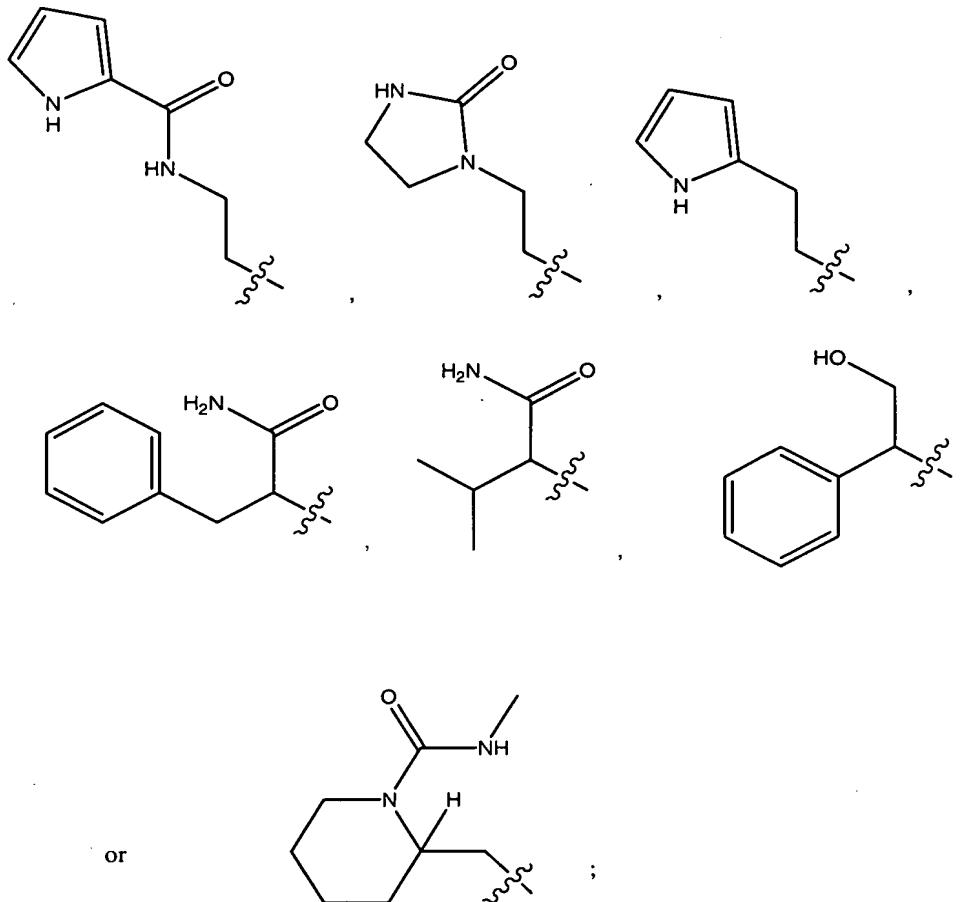
76. (Currently amended) A compound having the structure:



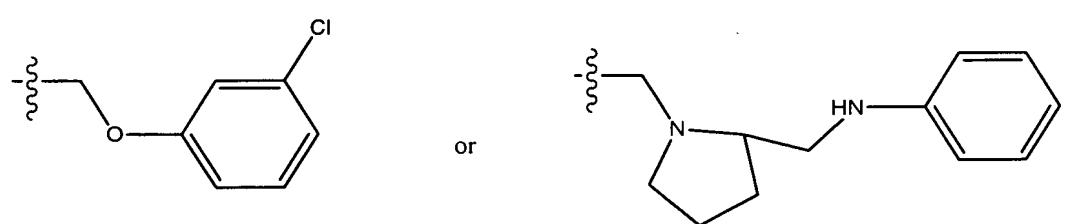
wherein R<sub>1</sub> is



Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 4



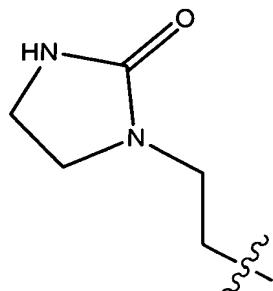
wherein  $R_5$  is H,  $CH_3$ , phenyl,



wherein  $R_6$  is H or  $CH_3$ ,

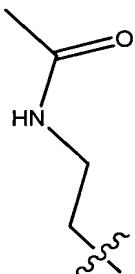
Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 5

and wherein when R1 is

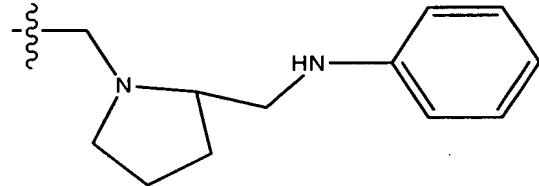


R5 is phenyl,

and wherein when R1 is

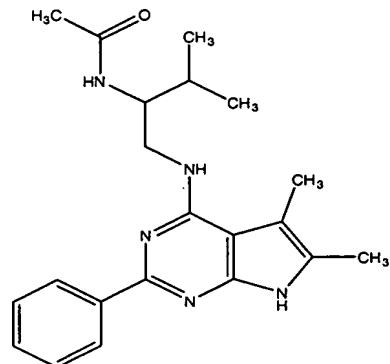


R5 is



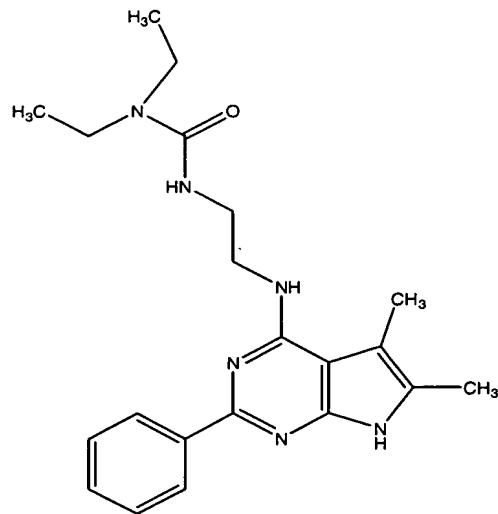
or a pharmaceutically acceptable salt thereof.

77. (Previously presented) The compound of claim 76, having the structure:

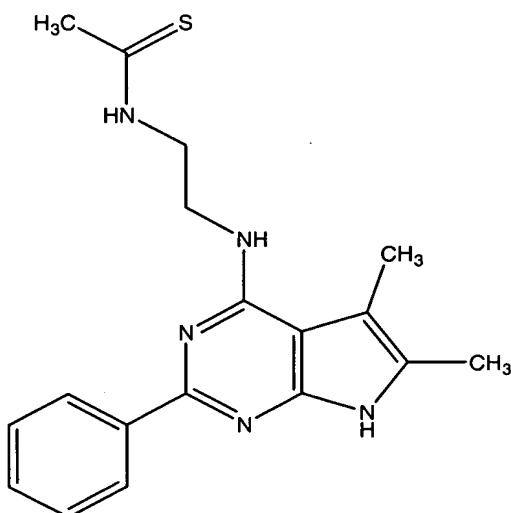


Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 6

78. (Previously presented) The compound of claim 76, having the structure:

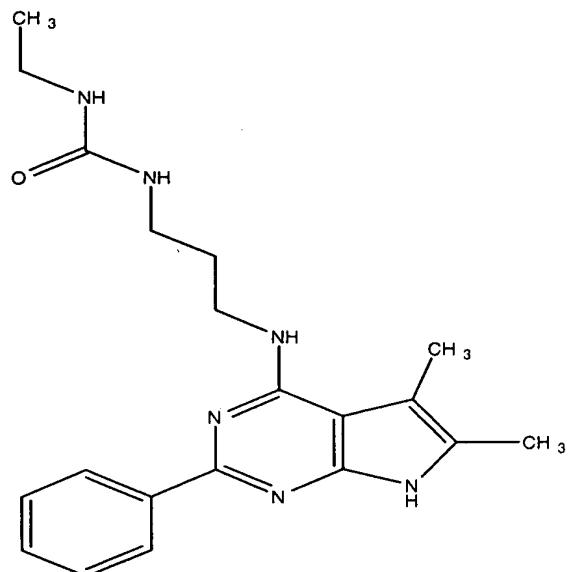


79. (Previously presented) The compound of claim 76, having the structure:

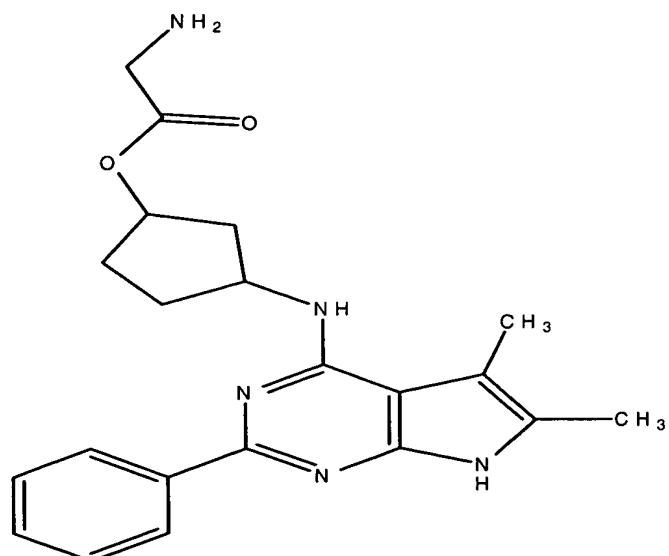


Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 7

80. (Previously presented) The compound of claim 76, having the structure:

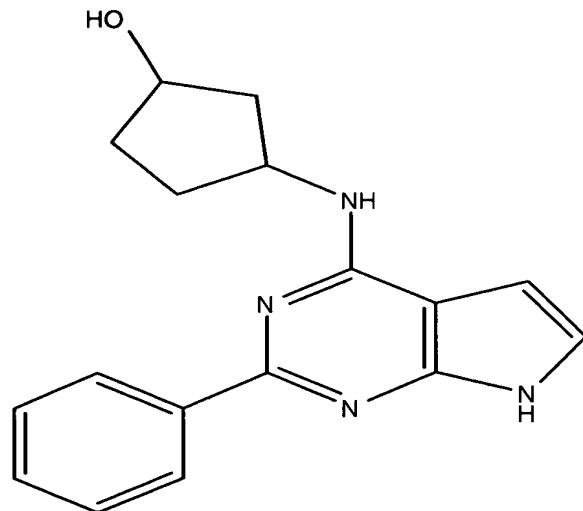


81. (Previously presented) The compound of claim 76, having the structure:

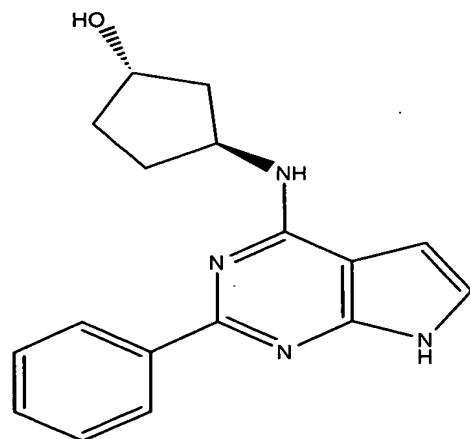


Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 8

82. (Previously presented) The compound of claim 76, having the structure:

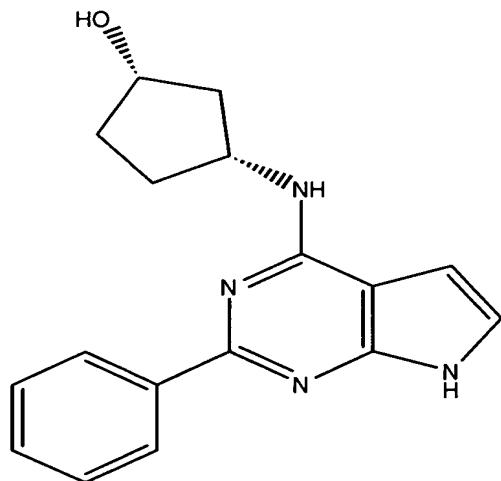


83. (Previously presented) The compound of claim 82, having the structure:

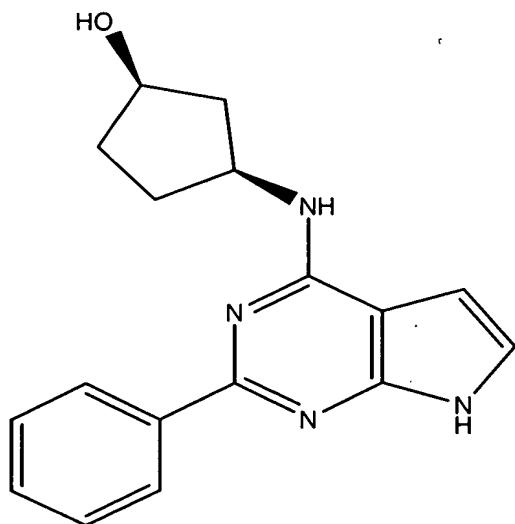


Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 9

84. (Previously presented) The compound of claim 82, having the structure:

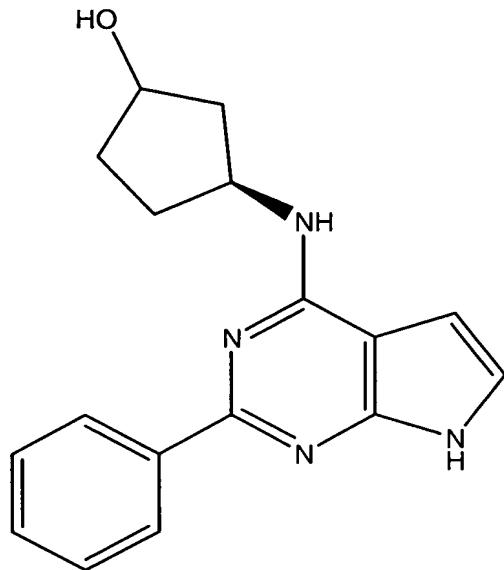


85. (Previously presented) The compound of claim 82, having the structure:

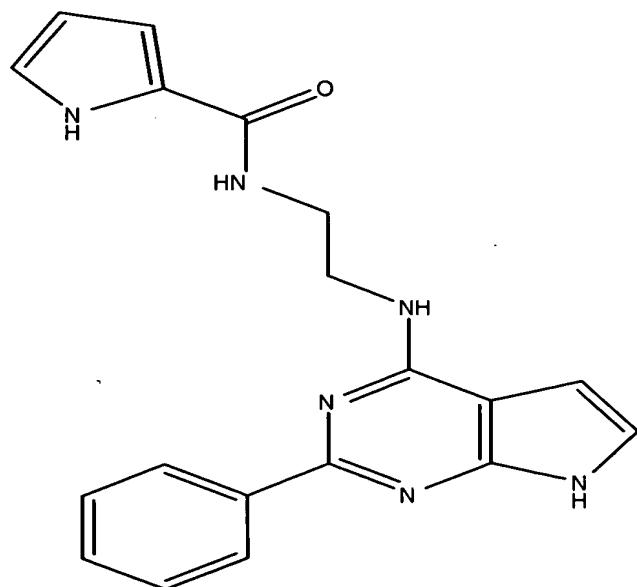


Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 10

86. (Previously presented) The compound of claim 82, having the structure:

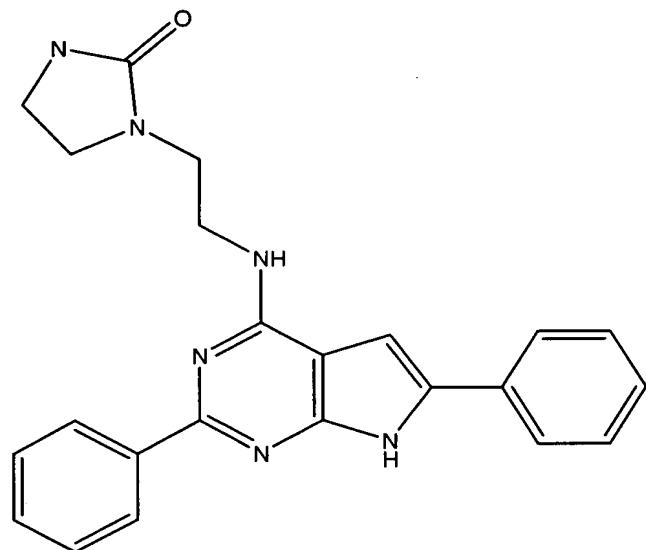


87. (Previously presented) The compound of claim 76, having the structure:

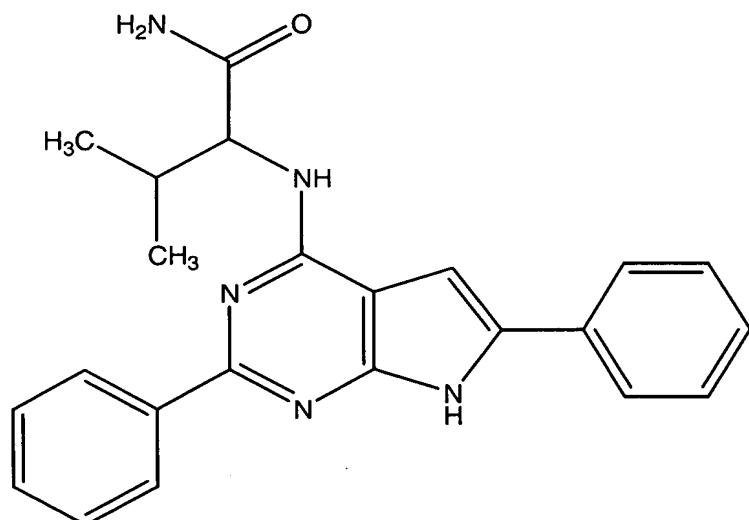


Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 11

88. (Previously presented) The compound of claim 76, having the structure:

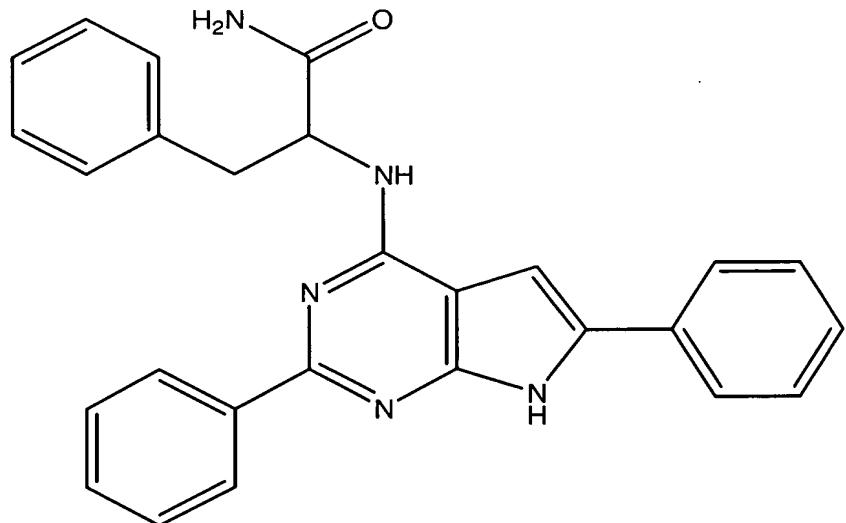


89. (Previously presented) The compound of claim 76, having the structure:

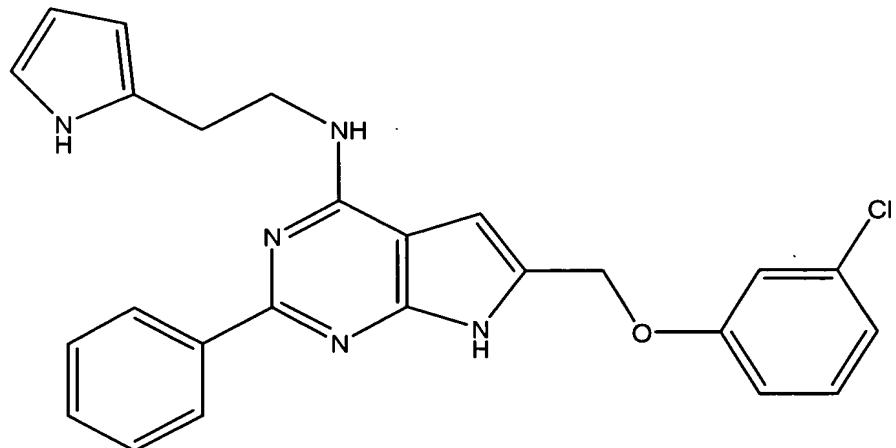


Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 12

90. (Previously presented) The compound of claim 76, having the structure:

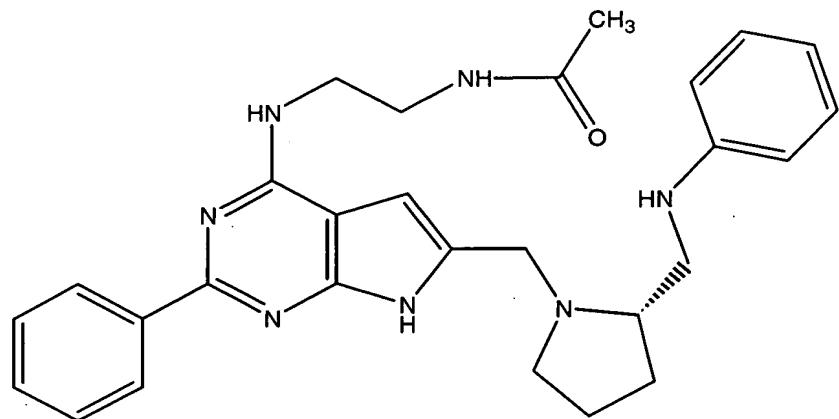


91. (Previously presented) The compound of claim 76, having the structure:

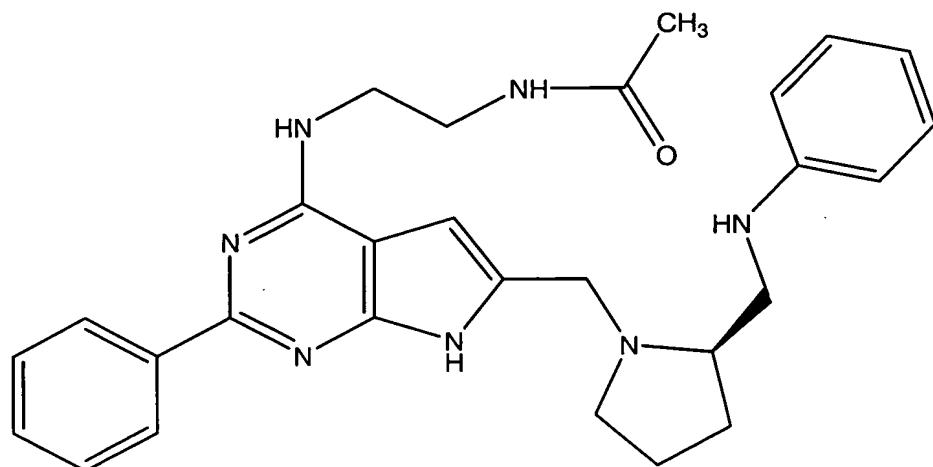


Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 13

92. (Previously presented) The compound of claim 76, having the structure:

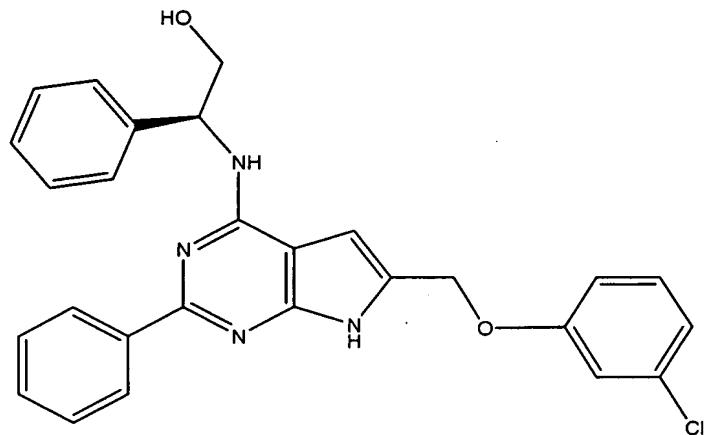


93. (Previously presented) The compound of claim 92, having the structure:

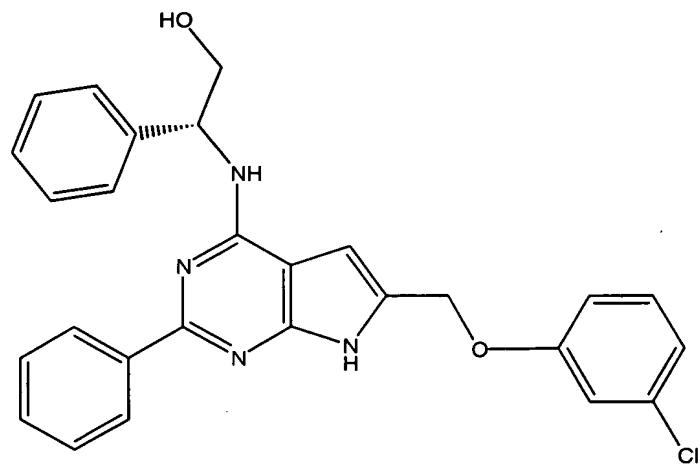


Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 14

94. (Previously presented) The compound of claim 76, having the structure:

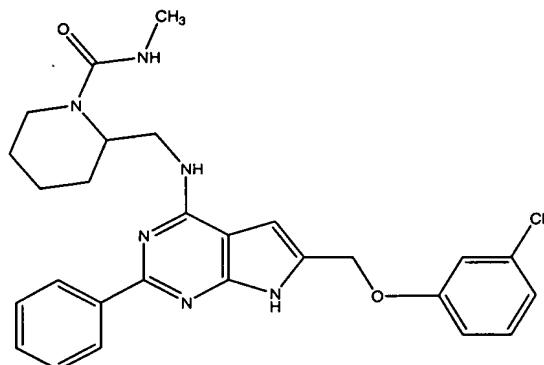


95. (Previously presented) The compound of claim 94, having the structure:

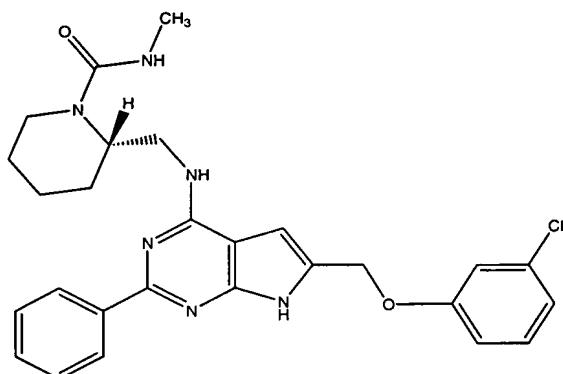


Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 15

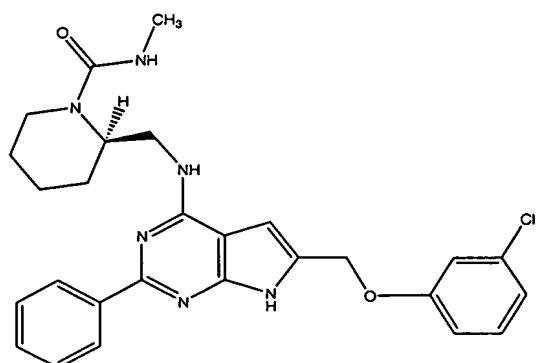
96. (Previously presented) The compound of claim 76, having the structure:



97. (Previously presented) The compound of claim 96, having the structure:

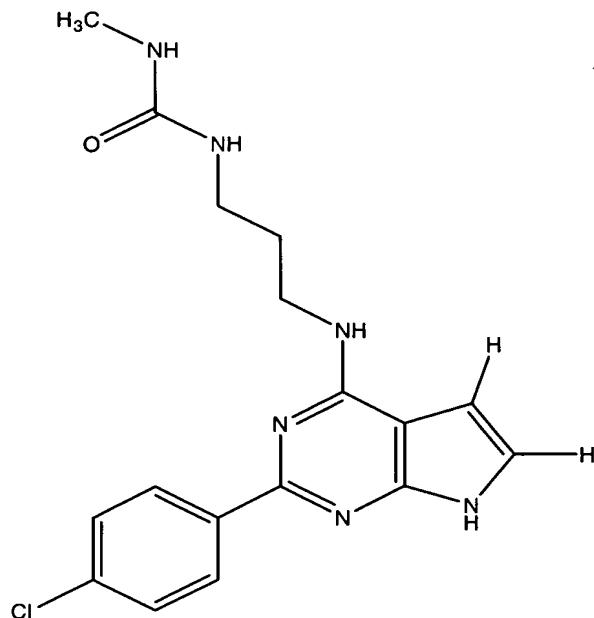


98. (Previously presented) The compound of claim 96, having the structure:



Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 16

99. (Previously presented) A compound having the structure:



100. (Previously presented) A method for treating a disease associated with an A3 adenosine receptor in a subject in need of such treatment, comprising administering to the subject a therapeutically effective amount of the compound of claim 76 or 99 so as to thereby treat the disease associated with the A3 adenosine receptor in the subject, wherein the disease associated with the A3 adenosine receptor is myocardial ischemia, bronchitis, or bronchoconstriction.

101. (Previously presented) The method of claim 100, wherein the subject is a mammal.

102. (Previously presented) The method of claim 101, wherein the mammal is a human.

103. (Previously presented) A prodrug of the compound of claim 76 or 99, wherein the prodrug is metabolized *in vivo* by a

human subject to an active drug which selectively inhibits the A3 adenosine receptor wherein the prodrug is an ester of an alcohol or carboxylic acid group, if such a group is present in the compound; an acetal or ketal of an alcohol group, if such a group is present in the compound; an N-Mannich base or an imine of an amine group, if such a group is present in the compound; or a Schiff base, oxime, acetal, enol ester, oxazolidine, or thiazolidine of a carbonyl group, if such a group is present in the compound.

104. (Previously presented) The prodrug of claim 103, wherein the prodrug is water-soluble.

105. (Previously presented) The prodrug of claim 103, wherein the prodrug is an ester of an alcohol group.

106. (Previously presented) A pharmaceutical composition comprising the prodrug of claim 103 and a pharmaceutically acceptable carrier.

107. (Previously presented) The pharmaceutical composition of claim 106, wherein said pharmaceutical composition is an ophthalmic formulation.

108. (Previously presented) The pharmaceutical composition of claim 106, wherein said pharmaceutical composition is an periocular, retrobulbar or intraocular injection formulation.

109. (Previously presented) The pharmaceutical composition of claim 106, wherein said pharmaceutical composition is a systemic formulation.

Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 18

110. (Previously presented) A method for inhibiting the activity of an A3 adenosine receptor in a cell which comprises contacting the cell with a compound of claim 76 or 99, so as to inhibit the activity of the A3 adenosine receptor.

Claims 111-113. (Canceled)

114. (Previously presented) A method for treating a respiratory disorder associated with an A3 adenosine receptor in a subject in need of such treatment, comprising administering to the subject a therapeutically effective amount of the compound of claim 76 or 99, so as to thereby treat the respiratory disorder in the subject, wherein the respiratory disorder is asthma, chronic obstructive pulmonary disease, allergic rhinitis or an upper respiratory disorder.

115. (Previously presented) The method of claim 114, wherein the subject is a human.

116. (Previously presented) A method for treating inflammation of the eye associated with an A3 adenosine receptor in a subject in need of such treatment, which comprises administering to the subject a therapeutically effective amount of the compound of claim 76 or 99 so as to thereby treat the inflammation of the eye in the subject.

117. (Previously presented) A method for treating a disease associated with an A3 adenosine receptor in a subject in need of such treatment, comprising administering to the subject a therapeutically effective amount of a compound of claim 76 or 99 so as to thereby treat the disease associated with the A3 adenosine receptor in the subject,

Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 19

wherein the disease associated with the A3 adenosine receptor is associated with mast cell degranulation.

118. (Previously presented) The method of claim 117 wherein the subject is human.

119. (Previously presented) A method for treating a disease associated with an A3 adenosine receptor in a subject in need of such treatment, comprising administering to the subject a therapeutically effective amount of a compound of claim 76 or 99 so as to thereby treat the disease associated with the A3 adenosine receptor in the subject, wherein the disease associated with the A3 adenosine receptor is asthma, glaucoma, retinopathy, ocular ischemia, or macular degeneration.

120. (Previously presented) The method of claim 119, wherein the subject is human.

121. (Previously presented) The method of claim 119, wherein the disease is asthma.

122. (Previously presented) The method of claim 119, wherein the disease is glaucoma.

123. (Currently amended) A pharmaceutical composition combination therapy for glaucoma, comprising the compound of claim 76 or 99, and a prostaglandin agonist,  $\beta$ 2 agonist, or a muscarinic antagonist.

124. (Currently amended) A pharmaceutical composition comprising ~~a~~ the compound of claim 76 or 99 and a pharmaceutically acceptable carrier.

Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 20

125. (Canceled)

126. (Canceled)

127. (Canceled)

128. (Previously presented) The pharmaceutical composition of claim 124, wherein said pharmaceutical composition is an ophthalmic formulation.

129. (Previously presented) The pharmaceutical composition of claim 124, wherein said pharmaceutical composition is an periocular, retrobulbar or intraocular injection formulation.

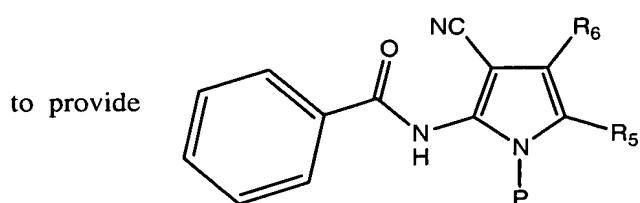
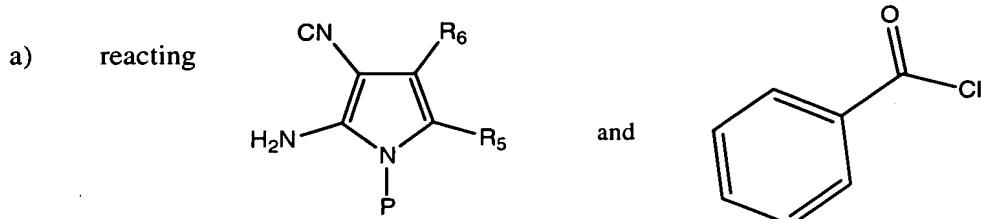
130. (Previously presented) The pharmaceutical composition of claim 124, wherein said pharmaceutical composition is a systemic formulation.

131. (Previously presented) The pharmaceutical composition of claim 124, wherein said pharmaceutical composition is a surgical irrigating solution.

132. (Canceled)

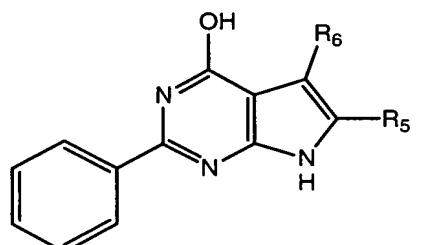
133. (Currently amended) A method of preparing the compound of claim 76, comprising the steps of

Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 21

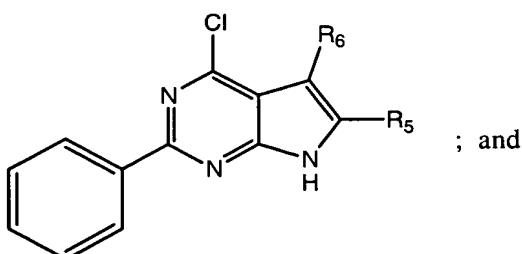


wherein P is a removable protecting group;

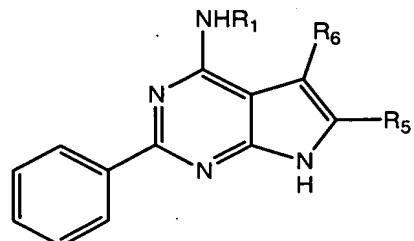
b) treating the product of step a) with acid in the presence of solvent to provide



c) treating the product of step b) with a chlorinating agent to provide

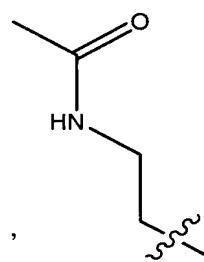
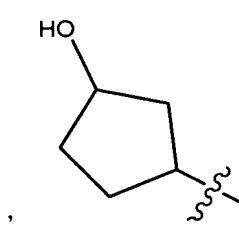
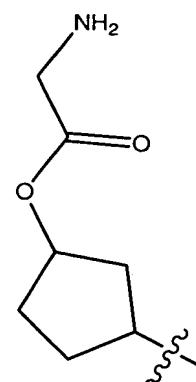
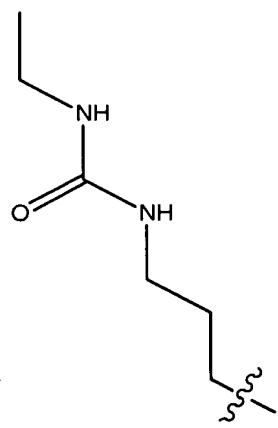
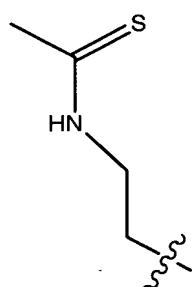
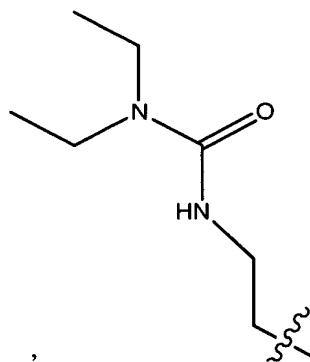
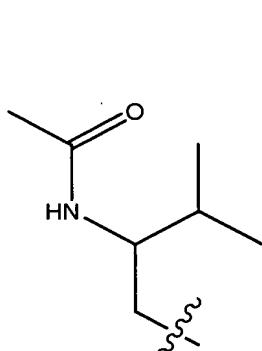


d) treating the chlorinated product of step c) with NH2R1 to provide

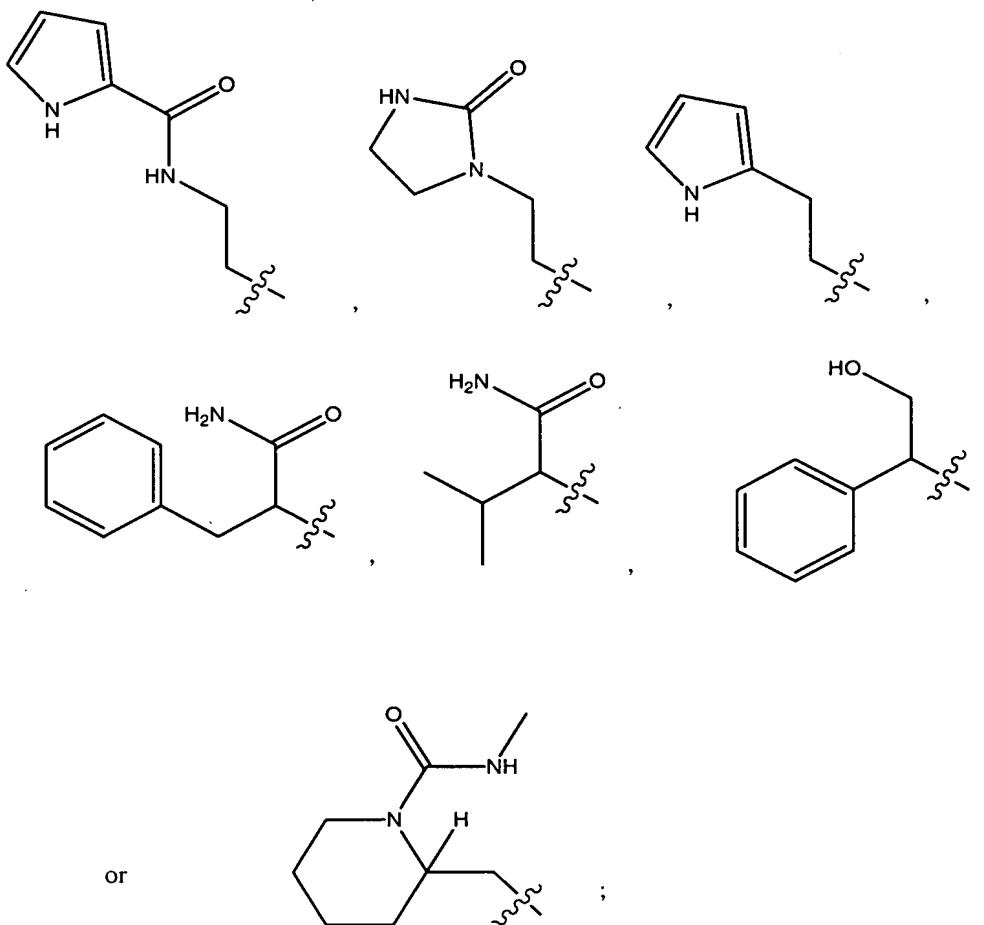


Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 22

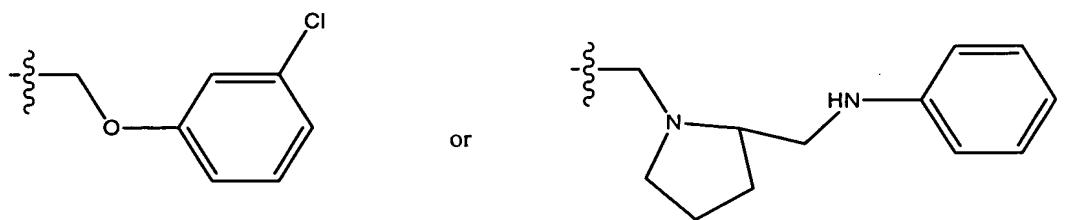
wherein  $R_1$  is



Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 23



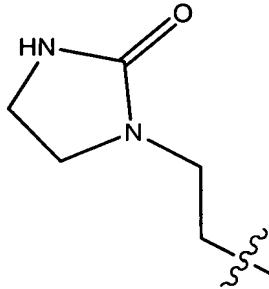
wherein R<sub>5</sub> is H, CH<sub>3</sub>, phenyl,



Applicants: Arlindo L. Castelhano et al.  
Serial No.: 09/728,616  
Filed : December 1, 2000  
Page 24

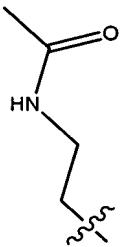
wherein R<sub>6</sub> is H or CH<sub>3</sub>,

and wherein when R<sub>1</sub> is

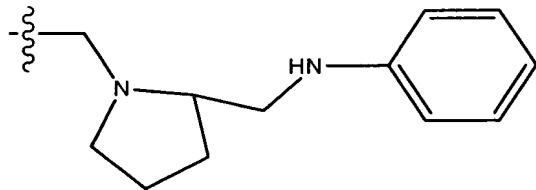


R<sub>5</sub> is phenyl.

and wherein when R<sub>1</sub> is



R<sub>5</sub> is



134. (Previously presented) The method of claim 133, wherein the acid of step b) is sulfuric acid, the solvent of step b) is methanol, and the chlorinating agent of step c) is POCl<sub>3</sub>.

135. (Previously presented) The method of claim 134, wherein step b) further comprises treating the compound with polyphosphoric acid.